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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/905,508	08/04/1997	LALEH SHAYESTEH	02307O-06772	5513

7590 05/10/2007

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
05/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/905,508	SHAYESTEH ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status

1. Claims 37-39 are pending.

Claims 37-39 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonjouklian et al (hereinafter referred to as Bonjouklian; US Patent 5,378,725; 1/3/1995), in view of Arnold et al (hereinafter referred to as Arnold; Genes,

Chromosomes, and Cancer, vol. 16, pages 46-54, 1996) and Volinia et al (hereinafter referred to as Volinia; Genomics, vol. 24, pp 472-477; 1994) and further in view of (in the alternative) Xiao et al (hereinafter referred to as Xiao, International Journal of Oncology; vol. 6, pp 405-411, 1995) or Skorski et al (hereinafter referred to as Skorski, Blood, vol. 86, pp 726-736, 1995).

Bonjouklian teaches and claims a method of treating PI3 kinase dependent neoplasms in mammals by administering non peptidic inhibitors (see col. 3, col. 4, table 1; col. 6, lines 49-60; and claims 1-9). Bonjouklian teaches that PI 3 kinase is an important enzyme in signal transduction with particular implications relative to the malignant transformation of cells (col. 2, lines 22-25). Bonjouklian specifically teaches a method for treating a phosphatidylinositol 3 kinase dependent condition in a mammal, such as abnormal cell growth as found in neoplasms, such as ovarian cancer, by administering a phosphatidylinositol 3 kinase inhibiting amount of a compound as shown in cols 2, 3, and 4 (col. 6, lines 49-col. 7, line 2). Bonjouklian teaches how to determine quantity of compound, such as wortmannin (an inhibitor of PI3 kinase phosphoinositide phosphorylation), to produce a desired therapeutic effect (col. 7, especially lines 54-62). It is noted that Bonjouklian does not specifically teach detecting the presence of an amplification of PIK3CA in ovarian cancer cells from a patient, however Bonjouklian does teach treating a "PI3 kinase dependent neoplasm" and it was known in the art at the time the invention was made that the region of chromosome 3q26 comprising PIK3CA was commonly amplified in ovarian tumors as taught by Arnold (see page 49, col 2, 3q26 is increased in 42% of cases) and Volinia. Arnold

specifically teaches that amplification of the 3q26-qter segment, which includes 3q26.3, suggests that the telomeric region of 3q contains one or more genes important in tumor initiation and/or progression (page 49, co. 2). Further, Volinia teaches that the catalytic p110 alpha subunit of PI 3 kinase (PIK3CA) is found in 3q26.3. Additionally, Xiao and Skorski teach that wortmannin, a known PI3 kinase inhibitor and taught by Bonjouklian as a treatment for a PI3 kinase dependent neoplasm, including ovarian cancer, was able to suppress growth of gastric cancer cells (see abstract of Xiao) and selectively inhibited the proliferation of leukemic cells (see pages 729 –730 and abstract of Skorski). Xiao teaches that growth of gastric cancer cell lines which exhibited elevated PI3 Kinase, MKN-45 and NUGC-4, was inhibited with wortmannin, while another gastric cancer cell line MKN-28, which did not exhibit such elevated PI 3 Kinase, was more resistant to wortmannin (see abstract, page 407, col. 2, first para, page 409, col 1 and 2). Further, Xiao teaches that the activation of PI-3 kinase appears to be required for oncogenic growth of these cells (see abstract). Skorski teaches that wortmannin inhibited the growth of leukemic cells (CML) which require PI 3 kinase for proliferation (see abstract, page 731, col. 2, lines 20-24).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made detect amplification of PIK3CA in ovarian cancer cells in a patient and to use the PI3 kinase inhibitor wortmannin to treat ovarian cancer as taught by Bonjouklian, because Arnold teaches that such region was commonly amplified in ovarian tumors and Volinia teaches that PIK3CA is found in 3q26.3. Therefore, from the combined teachings of Volinia and Arnold, the ordinary artisan

would been taught that ovarian cancer tumors would include those that had the region 3q26 amplified, including 3q26.3, suggesting that the telomeric region of 3q contains one or more genes important in tumor initiation and/or progression, as taught by Arnold, and that PIK3CA was found in the same region, as taught by Volinia. Given that Bonjouklian teaches treatment of PI3 kinase dependent neoplasms, such as ovarian cancer, the ordinary artisan would have been motivated to include ovarian tumors which were characterized by the amplification PIK3CA in the method of Bonjouklian because it was known in the art that PIK3CA was found at 3q26.3 and Xiao teaches that wortmannin, a known PI3 kinase inhibitor and taught by Bonjouklian as a treatment for a PI3 kinase dependent neoplasm, including ovarian cancer, was able to suppress growth of gastric cancer cells while Skorski teaches that wortmannin selectively inhibited the proliferation of leukemic cells (see pages 729 –730 and abstract of Skorski). Xiao teaches that growth of gastric cancer cell lines which exhibited elevated PI3 Kinase, MKN-45 and NUGC-4, was inhibited with wortmannin, while another gastric cancer cell line MKN-28, which did not exhibit such elevated PI 3 Kinase, was more resistant to wortmannin (see abstract, page 407, col. 2, first para, page 409, col 1 and 2). The ordinary artisan would have had a reasonable expectation of success that wortmannin, as taught by Bonjouklian, would be an effective inhibitor of the pathological proliferation of ovarian tumor cells with amplification of PIK3CA because wortmannin was known to inhibit growth of different cancerous cells which had elevated PI 3 kinase activity and were PI 3 Kinase dependent as taught by Xiao and Skorski.

5. Claims 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonjouklian in view of Daneshvar (Daneshvar et al; American Journal of Human Genetics, (1996) Vol. 59, No. 4 SUPPL., pp. A65, November 1996) and further in view of, in the alternative, Xiao or Skorski.

Bonjouklian teaches and claims a method of treating PI3 kinase dependent neoplasms in mammals by administering non peptidic inhibitors (see col. 3, col. 4, table 1; col. 6, lines 49-60; and claims 1-9). Bonjouklian teaches that PI 3 kinase is an important enzyme in signal transduction with particular implications relative to the malignant transformation of cells (col. 2, lines 22-25). Bonjouklian specifically teaches a method for treating a phosphatidylinositol 3 kinase dependent condition in a mammal, such as abnormal cell growth as found in neoplasms, such as ovarian cancer, by administering a phosphatidylinositol 3 kinase inhibiting amount of a compound as shown in cols 2, 3, and 4 (col. 6, lines 49-col. 7, line 2). Bonjouklian teaches how to determine quantity of compound, such as wortmannin (an inhibitor of PI3 kinase phosphoinositide phosphorylation), to produce a desired therapeutic effect (col. 7, especially lines 54-62). It is noted that Bonjouklian does not specifically teach detecting the presence of an amplification of PIK3CA in ovarian cancer cells from a patient, however Bonjouklian does teach treating a "PI3 kinase dependent neoplasm". Further, Danesvhar teaches that the catalytic subunit of PI3 kinase maps to a region of chromosome 26 which is amplified in ovarian cancer. Danesvhar teaches that the gene was increased in copy number in all tumor samples and cell lines tested and showed increased expression by immunohistochemistry in tumor cell lines (see abstract).

Additionally, Xiao and Skorski teach that wortmannin, a known PI3 kinase inhibitor and taught by Bonjouklian as a treatment for a PI3 kinase dependent neoplasm, including ovarian cancer, was able to suppress growth of gastric cancer cells (see abstract of Xiao) and selectively inhibited the proliferation of leukemic cells (see pages 729 –730 and abstract of Skorski). Xiao teaches that growth of gastric cancer cell lines which exhibited elevated PI3 Kinase, MKN-45 and NUGC-4, was inhibited with wortmannin, while another gastric cancer cell line MKN-28, which did not exhibit such elevated PI 3 Kinase, was more resistant to wortmannin (see abstract, page 407, col. 2, first para, page 409, col 1 and 2). Further, Xiao teaches that the activation of PI-3 kinase appears to be required for oncogenic growth of these cells (see abstract). Skorski teaches that wortmannin inhibited the growth of leukemic cells (CML) which require PI 3 kinase for proliferation (see abstract, page 731, col. 2, lines 20-24).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made detect amplification of PIK3CA in ovarian cancer cells in a patient and to use the PI3 kinase inhibitor wortmannin to treat ovarian cancer as taught by Bonjouklian, because Daneshvar teaches that the PIK3CA was commonly amplified in ovarian tumors and showed increased expression by immunohistochemistry in tumor cell lines. Given that the Bonjouklian patent is directed to treatment of PI3 kinase dependent neoplasms, such as ovarian cancer, the ordinary artisan would have been motivated to include ovarian tumors which were characterized by the amplification PIK3CA in the method of Bonjouklian because it was known in the art that PIK3CA was increased in copy number in ovarian cancer cells. The ordinary artisan would have had

a reasonable expectation of success that wortmannin, as taught by Bonjouklian, would be an effective inhibitor of the pathological proliferation of ovarian tumor cells with amplification of PIK3CA because wortmannin was known to inhibit growth of different cancerous cells which had elevated PI 3 kinase activity and were PI 3 Kinase dependent as taught by Xiao and Skorski.

6. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bonjouklian, in view of Arnold and Volinia, and further in view of Xiao or Skorski, as applied to claims 37 and 38 above, and further in view of Powis (Powis et al; International Journal of Pharmacognosy, vol. 33, pages 17-26, 1995).

The teachings of Bonjouklian, Volinia, Arnold, Xiao and Skorski are set forth above. Bonjouklian & Arnold & Volinia in view of Xiao or Skorski do not teach the PI 3 kinase inhibitor LY294002 for the inhibition of the pathological proliferation of ovarian cancer cells, although Xiao does teach that LY294002 is a PI 3 kinase inhibitor. However, Powis teaches that LY294002 is a selective PI 3 kinase inhibitor (page 20, col. 1, last sentence of first full para). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use LY294002 to inhibit PI 3 kinase activity in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski. The ordinary artisan would have been motivated to use LY294002 to inhibit PI 3 kinase activity in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski because it was known to be a selective inhibitor of PI 3 kinase activity as taught by Powis. The ordinary artisan would have had a reasonable expectation of

success that LY294002 could be used to inhibit the pathological proliferation of ovarian cancer cells in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski because LY294002 was known to be an effective inhibitor of PI 3 kinase.

7. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bonjouklian, in view of Arnold and Volinia, and further in view of Xiao or Skorski, as applied to claims 37 and 38 above, and further in view of June (US Patent 6632789).

The teachings of Bonjouklian, Volinia, Arnold, Xiao and Skorski are set forth above. Bonjouklian & Arnold & Volinia in view of Xiao or Skorski do not teach the PI 3 kinase inhibitor LY294002 for the inhibition of the pathological proliferation of ovarian cancer cells, although Xiao does teach that LY294002 is a PI 3 kinase inhibitor. However, June teaches that LY294002 is a preferred PI 3 kinase inhibitor (col. 5, lines 60-62) and teaches inhibiting a response, such as proliferation, by a T cell, using LY294002 (claims 1-19). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use LY294002 to inhibit PI 3 kinase activity in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski. The ordinary artisan would have been motivated to use LY294002 to inhibit PI 3 kinase activity in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski because it was known to be a preferred inhibitor of PI 3 kinase activity as taught by June. The ordinary artisan would have had a reasonable expectation of success that LY294002 could be used to inhibit the pathological proliferation of ovarian cancer cells

in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski because LY294002 was known to be an effective inhibitor of PI 3 kinase activity.

8. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bonjouklian, in view of Arnold and Volinia, and further in view of Xiao or Skorski, as applied to claims 37 and 38 above, and further in view Lavin (Lavin et al; Experientia, vol. 52, pages 979-994, 1996).

The teachings of Bonjouklian, Volinia, Arnold, Xiao and Skorski are set forth above. Bonjouklian & Arnold & Volinia in view of Xiao or Skorski do not teach the PI 3 kinase inhibitor LY294002 for the inhibition of the pathological proliferation of ovarian cancer cells, although Xiao does teach that LY294002 is a PI 3 kinase inhibitor. However, Lavin teaches that LY294002 is an effective PI 3 kinase inhibitor and abrogated the ability of NGF to prevent apoptosis in PC-12 cells, suggesting one important role of PI 3 kinase is to ensure cell survival by preventing apoptosis (986, col. 2, lines 18-25). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use LY294002 to inhibit PI 3 kinase activity in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski. The ordinary artisan would have been motivated to use LY294002 to inhibit PI 3 kinase activity in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski because it was known to be a selective inhibitor of PI 3 kinase and cell growth as taught by Lavin. The ordinary artisan would have had a reasonable expectation of success that LY294002 could be used to inhibit the pathological proliferation of ovarian cancer

cells in the method of Bonjouklian & Arnold & Volinia in view of Xiao or Skorski because LY294002 was known to be an effective inhibitor of PI 3 kinase and to abrogate the ability of a growth factor to prevent apoptosis.

Response to Declaration

9. The Gray Declaration under 37 CFR 1.132 filed February 28, 2007 is insufficient to overcome the rejection of the claims based upon 35 U.S.C. 103 as set forth in the last Office action because:

In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, (1) the nature of the fact sought to be established, (2) the strength of any opposing evidence, (3) the interest of the expert in the outcome of the case, and (4) the presence or absence of factual support for the expert's opinion.

(1) In the instant case, the nature of the fact sought to be established is whether or not the amplification of the relatively small genetic region which comprises the PIK3CA gene would be expected to lead to overexpression of the gene.

Dr. Gray states in point 5, without factual support, that the fact that 3q26.3 was overexpressed, would not lead one of skill in the art to conclude that amplification of PIK3CA leads to overexpression of PIK3CA. Dr. Gray further states that the mere presence would not predictably lead to a correlation of overexpression.

(2) There is significant evidence which opposes the conclusion of the Gray declaration. The attached Grimaldi declaration come to conclusions different than those of Dr. Gray. In the Dr. Grimaldi declaration at paragraph 4, Dr. Grimaldi notes

"Chromosomal aberrations, such as gene amplification, and chromosomal translocations are important markers of specific types of cancer and lead to the aberrant expression of specific genes and their encoded polypeptides, including over-expression and under-expression. For example, gene amplification is a process in which specific regions of a chromosome are duplicated, thus creating multiple copies of certain genes that normally exist as a single copy. Gene underexpression can occur when a gene is not transcribed into mRNA." Thus, Dr. Grimaldi is making an express connection between gene amplification and overexpression and gene translocation and underexpression. This supports the factual basis of the rejection, and opposes the conclusion of the Gray declaration, by noting that gene amplification is associated with over expression.

Second, the Daneshvar reference specifically connects ovarian cancer and PIK3CA. While Dr. Gray argues that a search of all of the genes located in the 3q26 region would be necessary in order to determine which gene is associated with ovarian cancer, this argument fails to address the Daneshvar reference, which specifically connects PIK3CA with ovarian cancer at 3q26. This teaching that the region is less than 2 Mb and that "Phosphatidylinositol kinase type 3, catalytic subunit, maps to this region and appears to be a candidate for the gene selected for by the amplification. It is increased in copy number in all tumor samples and cell lines tested to date, and shows increased expression by immunohistochemistry in tumor cell lines." This is direct evidence that not only is the region in which PIK3CA located amplified, but that PIK3CA itself is overexpressed and is a candidate gene.

This identification is further supported by the attached Ashkenazi declaration, which notes at paragraph 5 that "If gene amplification results in overexpression of the mRNA and the corresponding gene product, then it identifies that gene product as a promising target for cancer therapy". With the Daneshvar teaching that the PIK3CA gene is both amplified and the protein product has increased expression, Ashkenzi shows that the ordinary practitioner would have found the gene product to be a "promising target for cancer therapy".

Thus, the conclusory results of Dr. Gray are directly opposed by the Grimaldi and Ashkenzi declarations and the Daneshvar reference.

(3) Dr. Gray has a direct interest in the case as an inventor.

(4) There is no factual support for Dr. Gray's position. Dr. Gray does not present any data supporting the conclusion that PIK3CA is not a likely target. Even the data showing that there are multiple genes does not assist the case, because the prior art specifically identified PIK3CA as one of a limited set of candidate genes. In fact, Daneshvar identified PIK3CA as the only likely target in the amplified region. Consequently,

given the very strong data opposing the conclusion of Dr. Gray, derived from two declarations and the cited prior art, the declaration is not found persuasive.

Response to Arguments

10. Applicant's arguments filed January 8, 2007 have been fully considered but they are not persuasive.

Applicant relies upon the declaration of Dr. Gray to overcome the prior art. For the reasons given above, the declaration was not found sufficient to overcome the prior art rejections. Further, the case law does not support the position of Applicant. As reaffirmed recently in Pfizer Inc. v. Apotex Inc., 82 USPQ2d 1321 (Fed. Cir. 2007), the legal standard for "reasonable expectation of success" is provided by caselaw and is summarized in MPEP 2144.08, which notes "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , In re O'Farrell , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this factual case, there is express suggestion in the prior art of Daneshvar that PIK3CA is associated with ovarian cancer. There is further evidence as shown in the alternate rejection by Arnold that 3q26 was associated with ovarian cancer and Volinna shows that PIK3CA, a protein known to be associated with neoplasm by the primary reference, was located at this location. This sufficient for a reasonable expectation of success. The MPEP cites In re O'Farrell, which notes regarding "obvious to try" at page 1682, that,

> "In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g ., In re Geiger , 815 F.2d at 688, 2 USPQ2d at 1278; Novo Industri A/S v. Travenol Laboratories, Inc ., 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); In re Yates , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); In re Antonie , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach

> that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. In re Dow Chemical Co ., 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); Hybritech, Inc. v. Monoclonal Antibodies, Inc ., 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1 986), cert. denied , 107 S.Ct. 1606 (1987); In re Tomlinson ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966).

The court in O'Farrell then, affirming the rejection, notes " Neither of these situations applies here." For the instant case, it is clear that neither situations applies here either. This is not a situation where the prior art suggests varying a variety of parameters, since the prior art of Daneshvar directly points to the use of PIK3CA and even the prior art of Arnold and Volinna is drawn to a single parameter, the overexpressed gene. This single parameter is selected, based upon the data shown in the Gray declaration, from about 30-50 different genes in total. This number is similar in scope to the number of possible elements in Apotex, where there were about 50 different salts which could be tested. Thus, given the specific direction of Daneshvar to PIK3CA and the limited testing required even using Arnold and Volinna, this is not an "obvious to try" situation, but rather a situation where there is a reasonable expectation of success.

Finally, the Supreme Court, in KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007), broadened the standard of obviousness in this issue. The Supreme Court noted "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103." In the current case, the number of genes

located at 3q26 is a finite and very limited number, probably less than 50 genes in total. Thus, following the standard enunciated by the Supreme Court in KSR, selection of PIK3CA from 3q26, when directed to this region by Arnold and Volinna, and directed to this particular gene by Daneshvar, leads to anticipated success. However, even under the stricter Federal Circuit standard, there is a reasonable expectation of success.

The rejections are therefore maintained.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

5/9/07